Molecular communication over gas stream channels using portable mass spectrometry.

Stamatios Giannoukos, Alan Marshall, Stephen Taylor* and Jeremy Smith

Department of Electrical Engineering and Electronics, University of Liverpool, Brownlow Hill, Liverpool, L69 3GJ, United Kingdom

Short Title: Odor generation for information communication using MS.

*Corresponding author: e-mail: S.Taylor@liv.ac.uk

ABSTRACT

The synthetic generation/coding and transmission of olfactory information over a gas stream or an odor network is a new and unexplored field. Application areas vary from the entertainment or advertisement industry to security and telemedicine. However, current technological limitations frustrate the accurate reproduction of decoded and transmitted olfactory data. This study describes the development, testing and characterization of a novel odor emitter (OE) which is used to investigate the generation - encoding of gaseous standards with odorous characteristics with a regulatable way, for scent transmission purposes. The calibration and the responses of a developed OE were examined using a portable quadrupole mass spectrometer (MS). Experiments were undertaken for a range of volatile organic compounds (VOCs) at different temperatures and flow rates. Individual compounds and mixtures were tested to investigate periodic and dynamic transmission characteristics within two different size tubular containers for distances up to 3 m. Olfactory information transmission is demonstrated using MS as the main molecular sensor for odour detection and monitoring and for the first-time spatial encryption of olfactory information is shown.

1. INTRODUCTION

Transmission of odor as data over a gas stream or communication networks is a novel and interesting phenomenon. The integration of olfactory information into virtual reality or domestic environments alongside video and audio signals is an emerging technological field [1-5]. Data communications typically involves the spatial and temporal transmission of information. This requires a three-stage procedure which includes: a) the generation of a characteristic information carrier signal e.g. in the form of an electrical signal, an electromagnetic wave, a molecular species etc., b) the transmission or propagation of this information-carrying signal across space and time, and c) the reception and decoding of the message by a receiver (e.g. visual/audio sensor, electro-optical, or chemical sensor, etc.). Even though existing mainstream communication models are well established (e.g. radiowaves, acoustic waves, etc.), there are many areas where conventional communication approaches are inadequate and alternative novel communication solutions are required. The concept of olfactory data transmission over a scent network is such a scheme [6].

The transportation of chemical molecules or chemical signals over a distance within a physical network or environment is known as molecular communication [6-9]. In scent communications, odor molecules act as chemical carriers of information. They are released by an emitter and propagate over a physical medium to reach a receiver (e.g. chemical sensing system) for data detection and message decoding. Molecular communication can be used for both short and long range chemical communications [10-16]. In the natural world, microscale and nanoscale molecular communication schemes have been extensively observed in biological and biochemical systems or signaling procedures such as intercellular and intracellular processes [17-19]. In macroscale environments, chemical substances are utilized to transmit chemical information over long distances. Characteristic examples of both microscale and macroscale molecular communications in nature are pheromones which are

used for intra and inter species communications [20-31]. Pheromones can be used to convey information, to mark pathways (e.g. in insects), to locate food, to inform about potential dangers, to summon compatriots or even to inform populations about possible infectious diseases (e.g. as defense mechanism and rapid method of communication in plants or insect populations). For example, plants or trees infested by pests have been observed to produce specific volatile organic compounds (VOCs) - markers at certain quantities to chemically interact and alarm the healthy agricultural crop at ambient conditions [32]. The odor molecules produced contain chemical communication signals which propagate and their function benefits both sides (the sender and the receiver). In the animal kingdom, scent communications participate in mate selection and kin identification. An example of molecular communications in the aquatic environment is chemical communication among fish through specific pheromones for reproduction purposes (e.g. pheromone-containing urinary pulses in goldfish to attract a suitable partner) and for food localization and semiochemical responses [33]. In addition to pheromones, molecular chemical messengers or transmitters include: hormones, allomones, and kairomones [34]. All these are essential for regulating physiology, for affecting behavioral processes or for mediating interspecific interactions.

In macromolecular communications, the chemical characteristics (e.g. molecular weight, chemical structure, geometry, etc.) and physical and chemical properties (e.g. vapor pressure, boiling point, etc.) of the odor molecules (information carriers) affect the way they spread through a gas or aqueous phase medium [35-39]. In macromolecular scent communications, olfactory information is not simply one-factor dependent and can be encoded in the size, type, structure, nature or physicochemical properties (e.g. polarity) of the odorous chemical particle, its concentration, the time of release, the time of reception, its interaction with other compounds and the available receptors [40-42].

Accurate artificial scent communications depend on the exact analytical composition of odor molecules. Odors are mostly complex mixtures of volatile organic compounds (VOCs) originating from various chemical families/groups at different concentration levels, which interact in a synergistic or additive way [43]. Odor classification and decoding methodologies for qualitative and quantitative characterization of low and high volatility compounds utilize advanced instrumental methods for chemical analysis such as electronic noses (chemical sensor arrays with suitable pattern recognition systems) or mass spectrometry (MS) systems [43]. The latter could be stand-alone bench-top MS or hyphenated with other analytical technologies such as gas chromatography (GC) [44]. Solid phase microextraction (SPME) GC-MS [45-49], GC connected with electron capture detection (ECD) [50] sensors, GC x GC [50], GC coupled with olfactometric (O) detection sensors (GC-O), GC-MS-O [51-57], proton-transfer-reaction (PTR) – MS [58] and selected-ion-flow-tube (SIFT) – MS [43], has also been used for odor analysis and classification. Ion mobility spectroscopy (IMS) and ion mobility mass spectrometry (IMMS) are chemical sensory systems for selective VOC detection [43]. Electronic noses (e-noses) [43, 59] have been demonstrated based upon Surface Acoustic Wave (SAW) devices, quartz crystal microbalance (QCM) technology and metal oxide sensors. e.g. for VOC detection. Some of the above systems (e.g. QCM sensors) have also been used for moisture and inorganic gas detection during on-line monitoring.

Odor and/or VOC sample collection and introduction techniques are the primary analytical steps during the chemical analysis of odors and their precision critically affects the whole odor profiling process. Therefore, odor sample collection methodologies employ low-permeability, low-reacting, materials (e.g. stainless steel, polymer bags or special absorptive materials) to eliminate possible loss or contamination of the odorous information due to diffusion or absorption phenomena [43, 51].

All the above chemical sensorial approaches/measurements allow the compositional understanding of complicated odor matrices necessary to ensure a reliable sensory assessment of a product or an experience [51]. However, they do not provide information regarding human olfactory perception. This is essential especially during scent communications within virtual reality caves or during integration of scent generating devices in virtual reality goggles. Human olfaction is a dynamic procedure that involves the interaction of odorant molecules with the receptor neurons located in the olfactory epithelium [60-65]. Odorant molecules reach the nasal cavity by diffusion enhanced with a gentle or forceful sniffing airflow (flow assisted diffusion) though inhalation as part of the breathing process [61, 62]. Olfactory perception in humans is therefore linked with the breathing process (which is known to be a sinusoidal pattern of inhalations and exhalations) and the ability to sniff and identify active odorous compounds (stimulants) from various sources [65]. The factors which affect the sensation of smell are internal (e.g. genetic), external (e.g. environmental), molecular oriented (e.g. molecular chemical structure, physical and chemical properties – volatility, boiling point, lipid-solubility etc.). Human perception of odorant molecules depends on the odor threshold, the recognition threshold, the hedonic tone and the quality of the odor (e.g. pleasant or unpleasant) [51, 64].

Precise synthesis and production of individual or complex odors requires comprehension and knowledge of techniques employed in the generation of gaseous standard mixtures and the use of reference materials [66, 67]. This is essential for the development, testing and evaluation of new analytical processes and/or research pathways e.g. the transmission of olfactory information over networks for telemedicine and security applications or the inclusion of the sense of smell in virtual reality environments or virtual reality simulation chambers. The methodologies deployed for gas standard generation include: a) static techniques at elevated pressures (e.g. gravimetric, volumetric and manometric) or

atmospheric pressures (e.g. single or multiple chambers of constant or variable volumes), b) dynamic techniques (e.g. gas streams mixing, chemical reactions, permeation, diffusion, electrolysis, and evaporation) and c) combinatory approaches (e.g. exponential dilution) [66-83]. The most common laboratory techniques for generating gaseous standards (mainly for calibration purposes) utilize mixing of defined flows of gases from gas cylinders at different proportions, injection techniques of liquid or gas samples into the stream of a diluent carrier gas, permeation tubes, diffusion and evaporation methodologies.

This study was developed in the framework of a research project which investigates scent macromolecular communications over gas streams (e.g. virtual reality caves, entertainment halls, simulation environments, etc) and odor networks using MS as the main detection sensor. Thus, we developed, tested and evaluated an odor generation system (odor emitter) for the precise, repeatable and controllable emission and modulation of complex odorous information. The transportation of olfactory data across a confined communication medium (1, 2 and 3 meters of tubular chambers with different inner diameters) was also investigated for selected VOCs with different volatilities (e.g. from very low (limonene) to very high (cyclopentane) - Table 1). This selection was done to examine and to confirm that the developed technology and concept is not limited by the nature and properties of the selected VOCs and that it can be applied to diverse fields-applications. Odor detection, monitoring and analysis were done using a portable membrane inlet quadrupole MS. The selection of MS as a continuous molecular monitoring system was based on its ability for simultaneous qualitative, quantitative and spatio-temporal information provided in real-time or near real-time. Such versatile and accurate analytical information cannot be provided by other conventional analytical sensors such as e-noses due to technological limitations (e.g. device instabilities, false-positive or false-negative signals, lack of reproducibility, lack of selectivity, susceptibility to interference, saturation effects, etc.). The odor generation

methodology-mechanism developed in this work and the acquired data enhance and highlight research pathways for digital olfaction in medical, security, entertainment, and search and rescue robotic applications.

2. EXPERIMENTAL SECTION

2.1 Motivation and concept

The motivation behind this work is the development and the chemical investigation and characterization of novel analytical systems/methodologies for accurate and controllable odor generation and subsequently the exploration of macroscale communication approaches using mass spectrometry as the principal demodulator sensor. The system developed allows the qualitative and quantitative exploration of molecular communication schemes and embodies properties for consistent olfactory information encoding and production/release. Using this approach steps may be identified to overcome the technological limitations during transmission and reception of data-modulated odor streams. The overall concept behind this research is to examine the possibility to combine advances in olfactory technology with communication and information theories, which will lead to the development and establishment of a new wireless communication medium - the odornet.

In this context, we have developed, optimized, tested and evaluated an odor emitter (or odor gun) that can generate gaseous standards (either as pulses or as continuous flows) in a precise and repeatable way. Olfactory information has been transmitted over controlled gas stream networks within defined spaces. The measurements explore the factors which affect odor transportation with distance including molecular diffusion and convection, molar flux, odor propagation, losses of odorous data, distortion effects, signal attenuation, delay times, and synchronization issues [84, 85]. The target compounds investigated are presented in

Table 1. These compounds are of low molecular weight molecules (< 150 Da) and cover a wide range of volatility, which is an important factor in olfactory transmission.

Table 1. Summary of the compounds used in the testing process of the odor emitter during transmission experiments.

Compound	**CAS Number**	**Molecular weight**	**Vapor pressure (mmHg) at 20°C**	**Boiling point (°C)**	**Odor threshold in air (ppm)**
Acetone (*m/z* 43)	67-64-1	58.0791	181.72	56	13 - 20
n-Hexane (*m/z* 86)	110-54-3	86.1754	120.96	68	130
Cyclopentane (*m/z* 70)	287-92-3	70.135	317.8 at (25°C)	49	N.A.
Toluene (*m/z* 92)	108-88-3	92.1384	22	110.6	8
Limonene (*m/z* 136)	138-86-3	136.2340	1.425	176	0.2

N.A.: Not available

2.2 Chemicals

Acetone with purity higher than 99.8 % for HPLC was purchased from Sigma-Aldrich Company, UK. Hexane (99.0 %) was obtained from Fisher Scientific. Cyclopentane (reagent grade, 98 %), toluene (anhydrous, 99.8 %), (R)-(+)-limonene (97 %) and methanol (HPLC grade, purity >99.9 %) were provided by Sigma-Aldrich Company, UK. All chemicals were provided in the liquid phase and were stored at room temperatures prior to their use.

2.3 Odor Emitter Design

The odor emitter is based on the controlled evaporation of liquid chemical analytes and on their diffusion in a carrier gas stream (e.g. N_2 or synthetic air) [86]. The main components of the OE are: a) a mixing chamber (MC), b) three evaporation chambers (EC), in which liquid analytes are introduced through a side injection port sealed with a thermo- resistant septum,

c) four mass flow controllers (MFCs) for the accurate control of the flow rates within the MC and the ECs, d) an automation platform for the simultaneous digital control of the MFCs e) a laptop PC and f) three digital controlled heating mantles for maintaining stable temperatures within the ECs. A schematic diagram is shown in Figure 1. The odor emitter can control with high precision up to three individual chemical analytes or up to three sub-groups of chemicals with similar physical and chemical properties and has the potential for annexation of additional ECs for increasing the input of odorant information in the odor line.

The MC and the ECs were manufactured to an in-house design using stainless steel grade 303 (Merseyside Metal Services Ltd., UK) in the workshops of the University of Liverpool. The MC is a cylindrical shape chamber with length 70 mm and outer and inner diameter 30 mm and 12 mm respectively. The input and output port at the two end sides of the MC are two 6.35 mm Swagelok stainless steel fitting unions. Three 3.18 mm Swagelok stainless steel fitting unions on the side of the MC are used for the introduction of the chemical vapor flows generated within the ECs. Every individual EC has height of 26mm, outer diameter of 30 mm and inner diameter of 12 mm. The ECs connect individually to the MC with a 3.18 mm PFA tubing with total length 100mm each. PFA tubing was purchased from Swagelok Manchester, UK. A screwed (M4 x 10 mm knurled thumb screws, AccuScrews, AccuGroup Ltd.) detachable base plate enables the access to the internal part of the EC, where an absorptive tissue is placed. Sealing of the base plate onto the EC is achieved with a nitrile rubber O-ring (RS Components Ltd. UK) which has temperature durability between -30 ^{o}C and 120 ^{o}C. The absorptive tissue is an anti-static 100% cotton cloth with total area 100 mm^2 purchased from Farnell Elements Ltd, UK. Two 3.18 mm side-ports on the side of every single EC are used for sample injection and air flow manipulation. The sample injection port is sealed with a thermo-resistant septum (Thermogreen® LB-2 Septa provided by Sigma-Alrdich Company Ltd.) with diameter of 6.7 mm and allows the repeatable and direct loading of the liquid

analyte of interest within the EC using a micro-syringe. Each septum is conditioned to provide low bleed at temperatures up to 350^{o}C, sealing the sample injection port of each EC and maintaining stable flows during operation. A Hamilton® syringe, 700 series with cemented needle and volume 100µL is used for the sample introduction via the thermo-resistant septum into the EC.

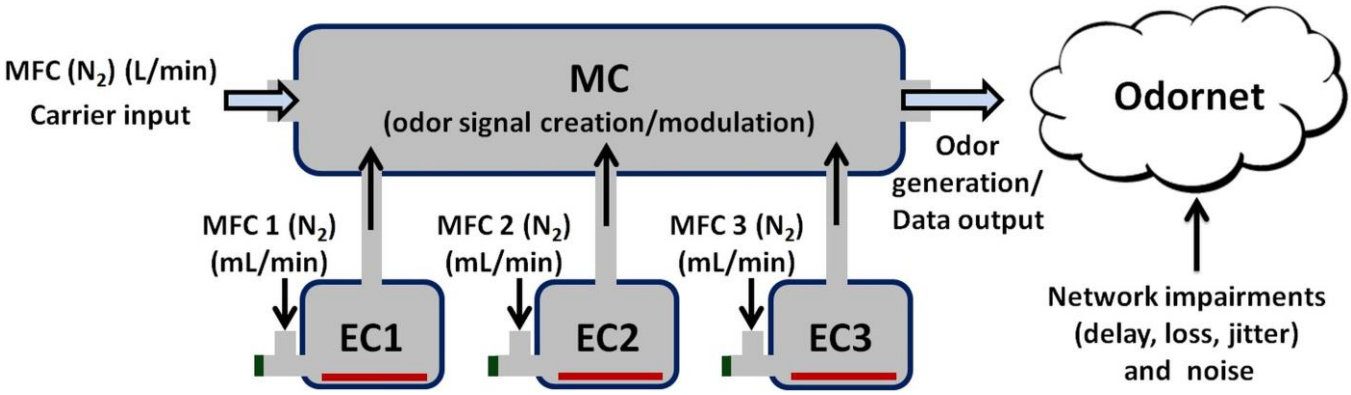

Figure 1. Schematic diagram of the odor emitter developed for the coding and transmission of olfactory information as data packages over physical and conventional odor channels - networks.

The MFCs (type GE50A) and the automation platform were purchased from MKS Instruments UK Ltd. All the MFCs were digitally calibrated for N_2 gas by the manufacturer. However, the MFC browser allows calibration and flow adjustment for a wide range of gases of choice. The MFC which controls the flow rate through the MC has full scale flow range between 0.5 and 10 L/min with 1 mL/min increments whereas the 3 MFCs which control the flow through the ECs have a flow range between 0.1 and 10 mL/min and 0.1 mL/min increments. The MFCs have fast response times of 500 ms with repeatable responses (± 0.3%). A function in the MFCs control software allows the real-time comparison of the set and actual flow rate value. The input pressure of the N_2 gas from the gas cylinder to the inlet of the MFCs is set constantly at 1.5 bar. The automation platform which controls the

sequences of the gas flows through the 4 MFCs is controlled by specially developed custom-made software in LabView 2015 32bit that enables their random synchronized operation. This means that the operator can set up automated recipes (program cycles) of unlimited sequences of time steps and flows for every individual MFC. The MFCs are the main components of the odor emitter and their functional and operational characteristics determine the rapid, precise and reproducible qualitative and quantitative production of a wide range of odors of interest. The heating mantles (DM-Series, model number DM-602) were provided by Medline Scientific Ltd. They have volume capacity of 250 mL and can provide controllably accurate and stable temperatures up to 400^{o}C which can be continuously monitored by a thermocouple. All the individual components of the odor emitting system were placed on a mobile platform at the same height with the reference detector allowing convenient transportation at different test distances.

2.4 Olfactory Test Channel

The olfactory test channel (OTC) used for these experiments was a tubular container acting as a transmission medium (communication channel) embedding the odor emitter and reference detector (MS) at each end. Using this arrangement, the phenomena governing the transportation of the olfactory information from the emitter to the receiver can be conveniently studied. Different size straight tubular containers with inner diameters 20 mm and 40 mm and lengths 1, 2 and 3 meters were used as OTCs. The containers were made from clear acrylic and were purchased from the Clear Plastic Shop, Chesterfield, UK at standard dimensions. During tests, the OTC tubing was supported with multiple laboratory retort stands (Rapid Electronics Ltd., UK) to ensure alignment of the odor emitter with the receiver.

2.5 Reference Detector

A portable membrane inlet mass spectrometer provided by Q-Technologies Ltd. UK [88] was the main sensor used to detect and continuously monitor the generated output signals of the odor emitter. The MIMS system has been described in detail previously elsewhere [88-91]. The main parts of the portable MIMS are: a) the membrane sampling probe that allows to the gas sample to pass through the membrane material into the MS for analysis, b) the triple filter quadrupole mass spectrometer - QMS (consisting of an EI ion source, mass analyzer and detector) and c) the vacuum system. The membrane interface is the principal unit for sample introduction into the MS. It utilizes a fine non-sterile flat polydimethylsiloxane (PDMS) membrane (Technical Products, Inc. of Georgia, USA) with membrane thickness of 0.12 mm and sampling area of 33.2 mm^2. The membrane is supported by a 0.8 mm thick stainless steel porous frit with 10 μm porosity. The distance between the membrane and the EI source is 50 mm. The EI ion source has a twin Thoriated Iridium filament assembly at 1.6 mA electron emission current and electron energy at 65 eV. The mass analyzer consists of a 125 mm main filter with a 25 mm small quadrupole filter at either end to which is applied RF only. It has a mass range of *m/z* 1-200 amu with 1 amu resolution and sensitivity of 1×10^{-4} A/mbar. The QMS employs two different types of detectors: a) a Faraday cup and b) a Channeltron type electron multiplier. The QMS system is enclosed in a stainless-steel chamber pumped down by a TURBOLAB 80 vacuum system obtained from Oerlikon Leybold Vacuum Ltd., Chessington, UK. The TURBOLAB 80 consists of an Oerlikon dual-stage oil-free DIVAC 0.8 T diaphragm pump and a TURBOVAC SL 80 H turbomolecular pump. The overall system pressure was continuously monitored using a digital pressure gauge (model: MRT 100 from Pfeiffer Vacuum Ltd., Newport Pagnell, UK) that uses a Pirani/Cold cathode method of measurement. Total base pressure of the system when the inlet valve is fully closed is 2.5×10^{-8} Torr. Operating pressure during experiments with the sample valve fully open and the

membrane sampling probe attached was stable between 1.0×10^{-6} Torr and 2.0×10^{-6} Torr. Data acquisition was done by a laptop computer, whereas data interpretation was performed using the combined Wiley 10^{th} with NIST14 mass spectral library. The multiple ion monitoring mode was selected to screen continuously characteristic mass fragments for the following chemical analytes of interest: acetone (*m/z* 43, 58), cyclopentane (*m/z* 42, 55, 70), n-hexane (*m/z* 56, 57, 86), toluene (*m/z* 91, 92) and limonene (*m/z* 68, 93, 136).

2.6 Calibration of the Reference Detector

For the determination of the analytical performance and accuracy of the developed odor emitter in the qualitative and quantitative production of odors of interest, a series of calibration measurements were performed using a portable MIMS based system. Our MIMS was additionally calibrated using two different techniques for gas standard production: a) a commercial gas generator (OVG-4 obtained from Owlstone Nanotech Ltd., UK) based on permeation tube technology and b) static dilution bottles.

The OVG-4 is part of an adaptable multi-module unit the GEN-SYS developed by Owlstone Ltd. UK [92] which hosts a series of systems with vapor and humidity generation capabilities. The OVG-4 incubates permeation tubes filled with chemical analytes of interest at determined temperatures and air/N_2 gas flows to produce chemical vapor standards with high accuracy. During our tests, zero grade N_2 gas with 99.998% purity purchased by BOC Gases Ltd., UK was used as a carrier input gas. A two-stage pressure regulator with stainless steel diaphragm was providing inlet gas pressure of 2.5 bars to the OVG-4 inlet. The main parts of the OVG-4 system is the carrier gas flow control system and the permeation oven chamber with its temperature controlling unit. The flow control unit utilizes a digital mass flow controller with gas flow range from 50 mL/min to 500 mL/min with 1 mL/min increment steps. The oven chamber is a reservoir that can host up to three permeation tubes. A permeation tube is a 6.35 mm diameter PTFE tubing with length 120 mm filled with a target

chemical analyte at a specific concentration. The two end sides of a permeation tube are sealed with 5 mm PTFE end caps and mild steel end crimps. The temperature range within the permeation oven chamber is between 30 ^{o}C to 100 ^{o}C with 0.1 ^{o}C increments. Calibration of the permeation tubes was done gravimetrically using a high accuracy mass balance. The OVG-4 can work in both split and split-less mode. Vapor production at standard concentration levels is achieved by the diffusion of a chemical analyte through the walls of a permeable tube (for a predetermined temperature) at constant rates over a carrier gas flow. The output of the OVG-4 is a 3.18 mm Swagelok compression fitting union directly connected to the MIMS inlet with a 50 mm 3.18 mm PFA tube. For this work, all the permeation tubes were made in house using a manufacturing kit provided by Owlstone Ltd. UK. Gas standards of the compounds of Table 1 were generated for MS screening at the following concentrations: 50ppb, 100 ppb, 250 ppb, 500 ppb, 750 ppb, 1 ppm, 5 ppm and 10 ppm.

The second technique that was used for gas standard production is the technique of the static dilution bottles. The procedure is based on McClennen et al. [66] and on Naganowska-Nowak et al. [67]. Liquid stock solutions of targeted chemicals in methanol were prepared in 10 mL screw vials (Agilent Technologies LDA UK Ltd.) at standard concentrations (both 200 and 1000 ppm each). Gas standards were prepared in 1.3 L and 2.8 L narrow-neck glass flasks (Sigma Aldrich Co. LLC., U.K.). The glass flasks were lidded with rubber stoppers with two injection ports (one for the liquid standard injection and the other for the dilution gas) and filled with zero grade N_2 gas purchased from BOC Gases, Ltd. UK. Appropriate quantities of each liquid stock solution, corresponding to their thermodynamic analogous standard gas phase concentrations in a defined volume of air, were injected with high precision micropipettes (Mettler-Toledo Ltd., Leicester, UK) in the glass flasks which were carefully lidded and covered with parafilm M wrapping film to eliminate sample loss. A 4-

hour phase of incubation at 60^{o}C was followed to allow complete evaporation of sample analytes and generation of gas standards. The glass flasks were carefully cleansed prior to the above process with deionized water (ReAgent Chemical Services Ltd, Cheshire, UK) and then heated at 80^{o}C overnight to eliminate possible VOCs contamination. Additionally, ten N_2 purging cycles (2 L/min) each followed to ensure purification. Random examination of selected glass flasks with the MIMS system followed to confirm external or remaining from previous tests VOCs absence. Once again gas standards of the compounds described in Table 1 were prepared at the following concentrations: 50ppb, 100 ppb, 250 ppb, 500 ppb, 750 ppb, 1 ppm, 5 ppm and 10 ppm. The generated gaseous standards were tested with MIMS-QMS system and mass spectra were recorded from the lowest to the highest concentration to avoid possible memory effects. The calibration measurements were replicated three times with both technique to ensure reproducibility and consistency of the results obtained. The experiments showed a repeatable degree of agreement and precision with a relative standard deviation (%RSD) of 5.1%.

Table 2. Summary of the R^2 values obtained by the calibration curves (from 2 different calibration techniques) for selected chemical compounds using Liverpool MIMS-QMS system.

Compound	**R^2 (OVG-4)**	**R^2 (dilution bottles)**
Acetone (*m/z* 43)	0.9981	0.9896
n-Hexane (*m/z* 86)	0.9990	0.9994
Cyclopentane (*m/z* 70)	0.9983	0.9982
Toluene (*m/z* 92)	0.9991	0.9991
Limonene (*m/z* 136)	0.9980	0.9981

Calibration curves of the MIMS system exhibited excellent linearity (Table 2) within the concentration range examined with R^2 values in the range from 0.9980 to 0.9994. Both techniques showed good agreement with each other.

2.7 Experimental Setup

A high purity N_2 carrier gas stream (0.5 - 10 L/min) pass through the MC to dilute at desired concentration levels the controllably generated (within the 3 ECs) vapour plumes of the analytes of interest. The 3 ECs allow the individual control of up to 3 characteristic analytes or sub-mixtures (components with similar physical and chemical properties) of a complex odor mixture. Vapor production within the ECs can be achieved by digitally controlled nitrogen gas flows (0.1 – 10 mL/min) and the applied temperature. The gas flow sequences applied in the MC and the 3 ECs are performed using an automation platform which allows random synchronized step changes. This allows the controlled release of specific chemical analytes through an EC to the MC and then to the reference detector inlet or to the communication channel and then to the MS for detection and on-line monitoring. Coupling of the outlet of the odor emitter with the OTCs was done using several layers of parafilm M wrapping film. The distance between the odor emitter and the reference detector or between the OTC and the reference detector was maintained at 10 mm. Temperature effects on the vapor production within the ECs were also investigated. Experiments were performed at ambient environment temperature (18 - 20 ^{o}C).

2.8 Experimental Design

The experiments were developed in two stages. The first experimental series included measurements carried out to investigate the analytical performance of the odor emitter during odour generation whereas the second stage dealt with odor transmission. For the evaluation of the developed system, the following factors were examined: a) air flow rates through the MC, b) air flow rates through the ECs, c) temperature variation of the ECs, d) liquid analyte

concentration levels within the ECs and e) selected physical and chemical properties of the tested chemical analytes (e.g. vapor pressure, boiling point, etc). Odor generation times were recorded and investigated in regards to the membrane sampling interface.

2.9 Sample Preparation

For testing the odor emitter, target chemicals in the liquid phase were injected within the ECs via a septum-sealed injection side port. Liquid stock solutions of the chemical analytes described in Table 1 were prepared in methanol in 5 mL vials at the following standard concentrations: 0.05 %, 0.1 %, 0.25 %, 0.5 %, 0.75 %, 1 %, 2 %, 5 %, and 10 %. Experiments with pure compounds at the purchased concentrations were also done. Nitrogen-forced chemical vapor flows of the compounds of Table 1, generated within the ECs, were introduced and mixed into the MC where a 1L/min N_2 carrier gas flow generated gaseous samples for release. The generation of the gas standard samples for the calibration of the MS and the quantification of the odor emitter output signals was described in detail above (section 2.6).

2.10 Sample Introduction

Sample introduction into the vacuum system of the MS was done though a permeable silicone membrane inlet sampling probe. The description of the membrane probe can be found in detail in the section 2.5 and in literature [90, 91]. The N_2 gas flow carrying the sample analytes and applied onto the membrane material was between 0.5 L/min to 5 L/min, depending on the test.

3. RESULTS AND DISCUSSION

3.1. Testing of the odor emitter

To investigate the analytical factors which affect the performance of the odor emitter, experiments were conducted with a) alterations of the flow rates through the MC and the

ECs, b) various concentration levels of the injected liquid analytes within the ECs, c) various temperature levels of the ECs.

Carrier gas flows through the MC and the ECs This experimental series examines the effects of various N_2 flow rates passing through the MC and the ECs of the odor emitter onto the generated chemical-odor signals. Therefore, a multiple-level dynamic flow approach was developed. The output of the odor emitter was approximately 10 mm far from the inlet of the MS. Produced gas emissions were flowing directly onto the membrane interface of the reference detector (MS) for direct analysis. Experiments with constant flows via the MC and via the ECs were conducted independently. The general recipe followed was for standard N_2 flow (L/min) through the MC, the N_2 flow through the EC was 0, 1, 0, 3, 0, 5, 0, 10, 0 mL/min sequentially. The duration for each flow step was 120 s. Injected sample quantity within the EC was constantly 50 uL per compound (at the purities provided by the supplier) and per test. All the experiments were done at ambient temperature. Representative results for acetone are shown in Figure 2. Increase of the flow rates passing through the MC present an exponential signal distribution. Characteristically for acetone this can be described by the following equation: $y = (3 \times 10^{-8}) e^{-0.461x}$. The detection time is defined as the time when signal current changes are first observed by the MIMS system by the reference detector when the N_2 flow through the MC was 1 L/min and the output of the odor emitter was directly connected to the inlet of the MS. Table 3 shows detection times for each chemical analyte (of Table 1). Table 3 also presents the R^2 values of the exponential curves of each compound tested which were obtained by altering the N_2 flow through the MC. Also shown are the linear regression coefficient values obtained from the relationship between the N_2 flows passing through the EC and the mass spectrometric detected chemical signals.

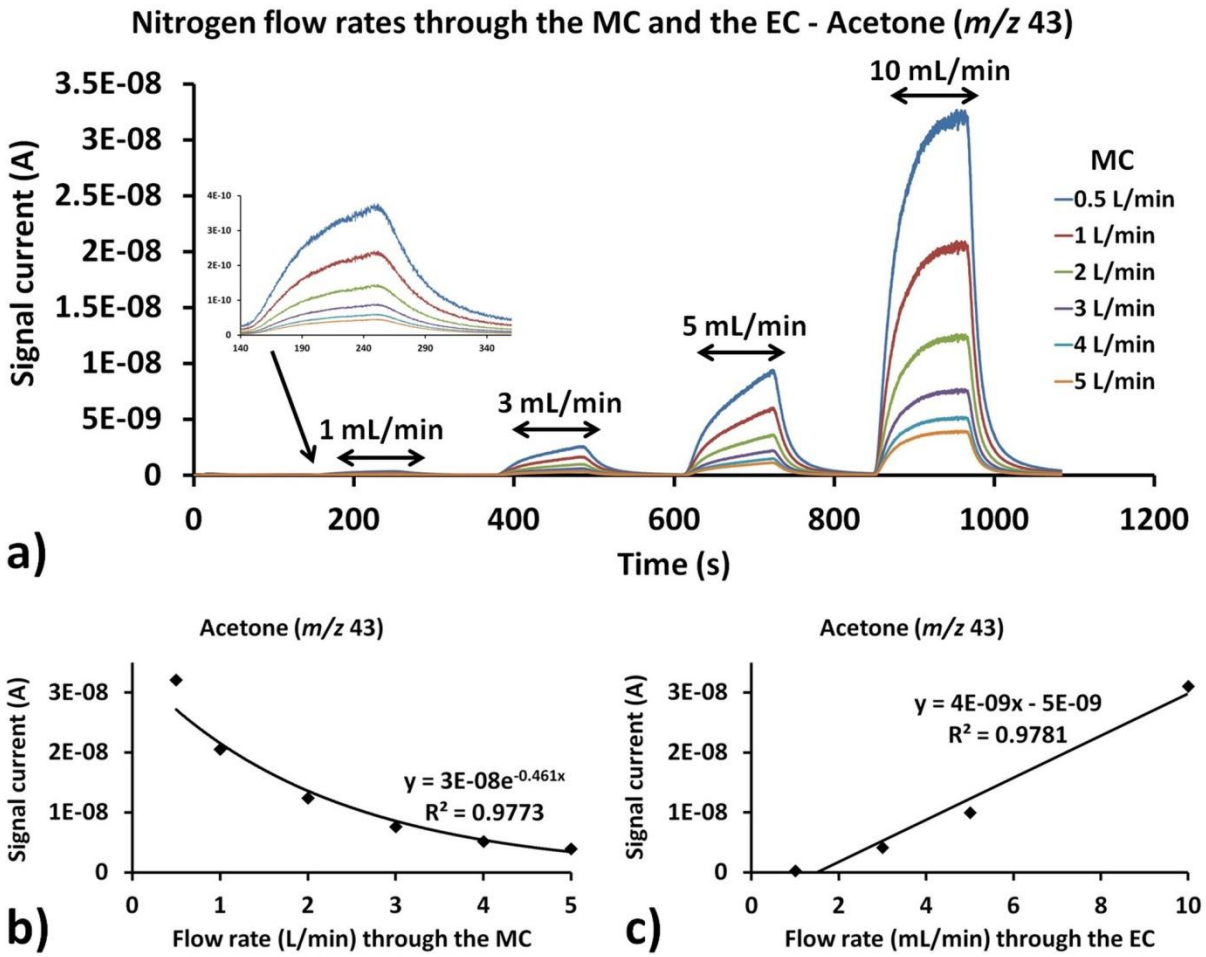

Figure 2. a) Measured signal current at the MIMS-QMS detector versus time as a function of Nitrogen flow rates. The measured currents are for single ion monitoring of the mass fragment *m/z* 43 (representative of acetone) for various N_2 flow rates through the MC and the EC. For a constant flow through the MC (0.5, 1, 2, 3, 4 and 5 L/min) the flow rate pattern through the EC is 0, 1, 0, 3, 0, 5, 0, 10, 0 mL/min, b) The effect of gradually increasing N_2 flows through the MC on the signal current of acetone, c) Linear signal current variation of the mass fragment *m/z* 43 of acetone with N_2 flow rate changes through the EC.

Table 3. Summary of the detection times (at 10 mm distance) and linear regression coefficient values (R^2) obtained from the calibration plots for the examined flows through the MC and the EC.

Compound	**Detection time (s)**	**R^2 (MC) (exponential)**	**R^2 (EC) (linear)**
Acetone (***m/z* 43**)	15	0.9773	0.9781
n-Hexane (***m/z* 86**)	20	0.9689	0.9855
Cyclopentane (***m/z* 70**)	14	0.9765	0.9957
Toluene (***m/z* 92**)	23	0.9968	0.9998
Limonene (***m/z* 136**)	25	0.8142	0.9659

Liquid analyte concentration levels within the ECs. In order to determine how the concentration of a liquid analyte within an EC affects the generated output concentration signals of the odor emitter a series of tests took place. During these experiments, 100 μL of each chemical analyte of Table 1 and at concentration levels of 0.05 %, 0.1 %, 0.25 %, 0.5 %, 0.75 %, 1 %, 2 %, 5 %, and 10 % were injected within the ECs and their signal outputs investigated (Figure 3). The N_2 gas flow passing through the MC was kept constant at 1 L/min. Individual step duration was 120 sec. Periodic odor release pulses through the EC were generated with the following sequence: 0, 10, 0, 10, 0, 10, 0 mL/min. This resulted in repeatable production of pulses with an average relative standard deviation (RSD) calculated to be 3.55 %. Output signals showed good linearity. The distance between the odor emitter and the MS inlet was again 10 mm. Comparison of the signals generated by the odor emitter with the signal values obtained from the calibration curves for each chemical analyte may be used as a concentration prediction tool. For example, for 10 mm distance between the OE and the reference detector and 1 L/min N_2 flow through the MC and 10 mL/min N_2 flow through

the EC of 0.05% concentration of acetone sample loaded in the EC, the OE generates an output concentration of 217 ppb.

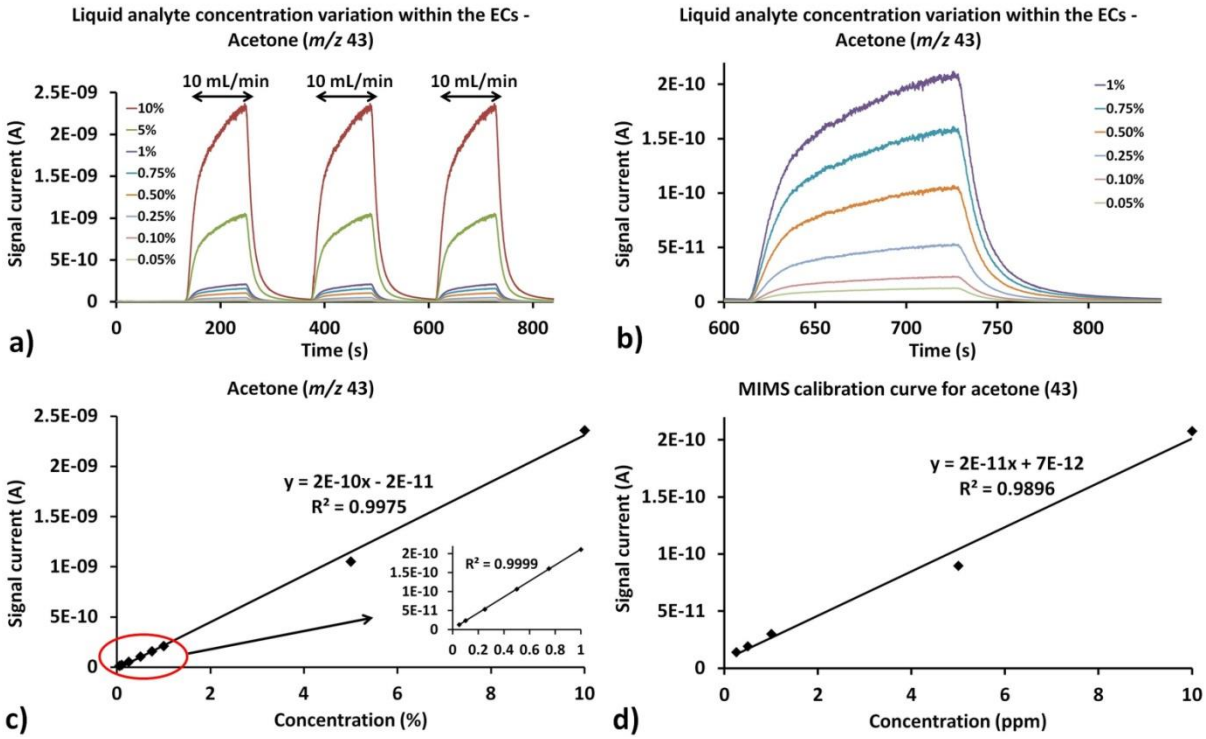

Figure 3. a) and b) Odor emitter output signals for acetone samples at various concentration levels. Flow rates through the MC and the EC were 1 L/min and 10 mL/min respectively. c) Calibration curve of the OE for various concentration samples of acetone (*m/z* 43) injected within the EC obtained from the MIMS system. Sample quantity was 100 μL per test. d) Calibration curve of the reference detector for acetone (*m/z* 43), obtained with the technique of the static dilution bottles.

Table 4. Summary of the linear regression coefficient values (R^2) obtained from the calibration plots for the examined concentration area (0.05% - 1%) for selected compounds.

Compound	**R^2**
Acetone (***m/z* 43**)	0.9999
n-Hexane (***m/z* 86**)	0.9988

Cyclopentane (***m/z* 70**)	0.9986
Toluene (***m/z* 92**)	0.9997
Limonene (***m/z* 136**)	0.9976

Temperature variation experiments. The effect of alternating the temperature of the evaporation chambers was also investigated. Tests were done at the following temperatures: 20 ^{o}C, 40 ^{o}C, 60 ^{o}C and 80 ^{o}C (Figure 4). The temperature rise has shown to have a positive effect on the detected signal intensity of the mass fragment under investigation. This is because increase of temperature enhances the evaporation of the chemical analytes within the evaporation chambers and provides a homogenous evaporation plume.

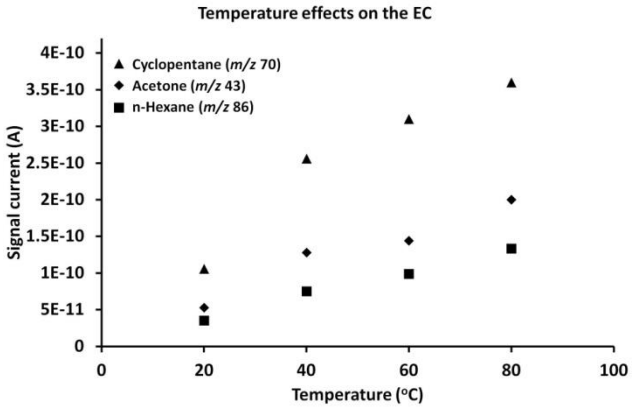

Figure 4. Temperature effects on the ECs of the odor emitter. Detected signal for cyclopentane (*m/z* 70), acetone (*m/z* 43) and n-hexane (*m/z* 86) showed one order of magnitude increase for the temperature range examined.

3.2. Olfactory information transport experiments

This experimental series examines odor transfer phenomena within two different size semi-open tubular containers (with inner diameters: 20 mm and 40 mm) and for distances 1, 2 and 3 meters for the individual analytes of the Table 1. Representative results for acetone are

presented in Figure 5. Similar transmission profiles were found for the rest of the compounds tested. Acetone signals generated by the odor emitter when it is directly connected with the inlet of the MS were considered to be the reference signals. For the distances examined (1, 2 and 3 m) the generated signals presented short dispersive profiles and showed sample loss at the receiver side. The propagation of the olfactory plume (signal) decays exponentially with characteristic distance dependent upon the tube geometry. For acetone propagating in a tube with internal diameter of 20 mm the propagation equation can be described by $y = A_0\, e^{-0.351x}$ whereas for a 40 mm ID tube is $y = A_0\, e^{-0.93x}$, where $A_0 = 2*10^{-8}$ and x is the distance between the OE and the reference detector. The degree of distortion of the olfactory signal and subsequently the signal loss is proportional to the length of the tube. This is analogous to the attenuation of a rectangular voltage pulse propagating along a transmission line. Increase of the gas flow (forcing function) through the MC results in faster transmission of molecular species. Moreover, the membrane inlet affects the detection of a chemical signal. Membrane rise and fall time can be measured prior to odor transmission and can be subtracted from the signal detection time to offer information about the propagation time of the olfactory information. A MS with a sinter leak or with real time monitoring capabilities could offer square shape pulses which are essential-ideal for communication signal analogies.

By altering the analytical parameters – operational conditions of the OE at a certain position in the space, molecular transmission can be achieved and predicted with precision over a certain distance. This information is especially important in virtual reality environments or security applications and allows to comprehend how odor signals distribute within gaseous media from the stage of their emission to the stage of their detection and decoding by a receiver. Signal decay in semi-open environments is expected due to factors such as noise, temperature, wind, etc.; arising from the transmission medium. However, the experiments in this section show that multiple OEs in series could be used at certain positions

to transmit and maintain stable olfactory information over very long distances, creating in such a way a network of olfactory antennas.

In the case of chemical transmission of complex mixtures, individual compounds can be discriminated and continuously monitored by multiple ion monitoring (e.g. 2 or 3 characteristic mass fragments per compound) which will ensure limited interferences. A system with MS/MS capability could also be used as a second stage of molecular identification-confirmation and could enhance the online monitoring process.

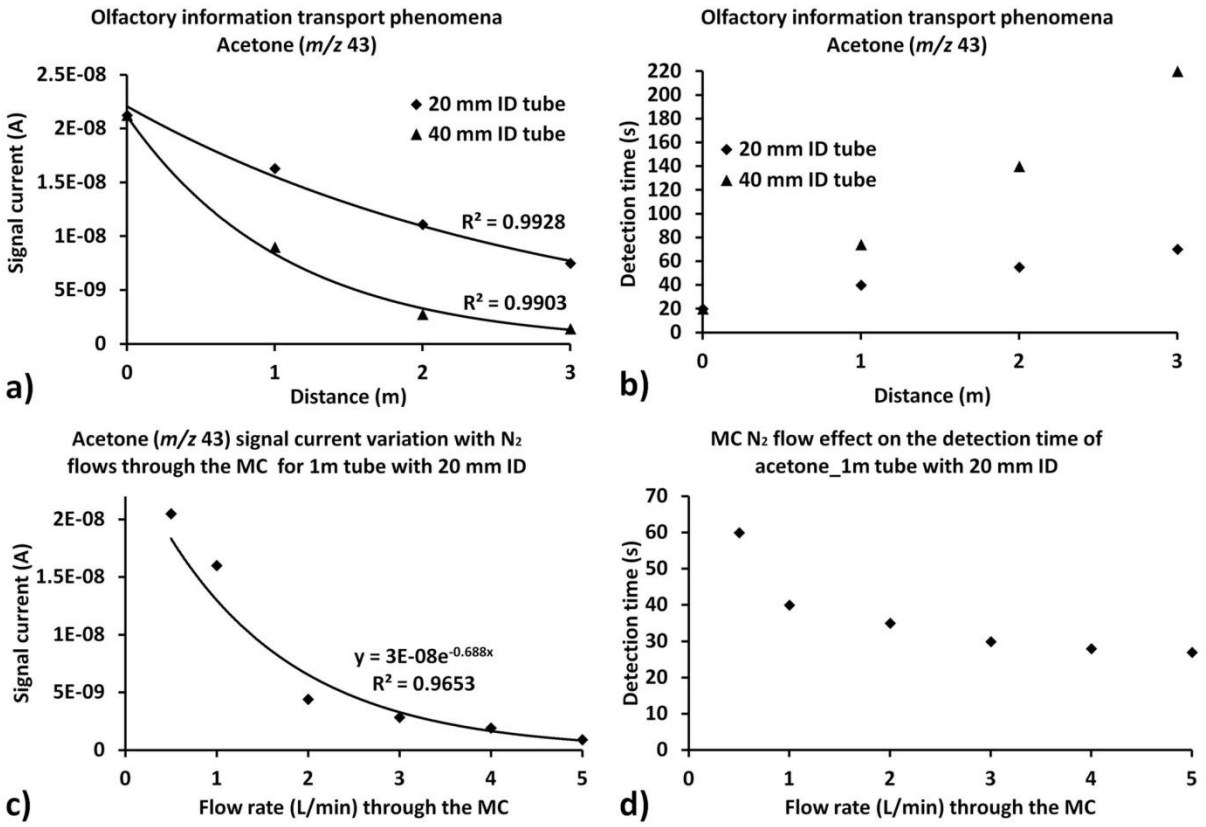

Figure 5. a) Experimental data obtained from the transmission of acetone molecules within a tubular container (pipe) with ID of 20 mm and 40 mm and over distances of 1, 2 and 3 m, b) Acetone detection time by the MIMS system during its transmission over a N_2 gas flow of 1 L/min through the 20 mm and 40 mm for distances up to 3 m, c) Effect of gradually increasing N_2 flows through the MC on the signal current of acetone molecules during

transmission experiments within a tubular container with ID of 20 mm and distance 1 m. Increase of the flow rate via the MC presents an exponentially decaying signal distribution, d) Increasing flow effects via the MC on the detection time of the transmitted olfactory information within a tubular container with ID of 20 mm and distance 1 m.

3.3. Synchronization experiments

The experiments described in this subsection aim to show that a vapor (e.g. acetone, toluene, etc) transmitted into a confined space in a certain direction can be used to encode information. For example, the vapor concentration could correspond with a particular information level. A confined environment (i.e. no leaks) is effectively a closed system. Quantities of vapor injected into the system will permeate throughout its space. For a given position of odor emitter, each point in space of this environment has a different concentration of the vapor and therefore a different information level. The vapor concentration at any point depends on the following factors: a) the source of the vapor (i.e. the odor emitting system, including direction-angle the emitter with regards to the receiving point, the emitted concentration and flow rate, the number and type of the chemicals used and their physicochemical properties); b) the communication channel (confined environment) its geometry and its thermodynamic properties such as temperature, humidity and pressure.

The experiments below demonstrate how a changing olfactory signal in space and time can be used to convey information. One application of this could be a physical layer encryption key in a macro-scale molecular communication scheme. Such a key could be used to lock, certify or encrypt data shared from a transmitter to a receiver. The unique chemical information coded in the vapor concentration transmitted between the sender and the receiver (positioned at a predetermined location in the closed environment space) ensures secrecy. As a further refinement, a molecular encryption key can be envisaged dependent upon

characteristic mass spectral fragments of a particular substance. In this case, mass fragment signal intensities, rather than total vapor concentrations are monitored at a particular location in space and time.

As mentioned previously, the emitter described in this study can generate and control odor pulses comprising of up to three different chemical analytes or up to three different chemical groups with similar physical properties and behaviors. In our experiments three compounds (cyclopentane, acetone and toluene) with different volatilities (Table 1) were selected for transmission within a 20 mm ID tube over a distance of 2 m. The 2 m distance was randomly selected to enable us to investigate molecular transportation in shorter and in longer tube distances. A volume of 20 uL of each analyte was injected within the three evaporation chambers (each chemical to its dedicated EC) prior to each test. Remaining chemical residues in the ECs among tests were purged with N_2 and heating at 100^{o}C. The N_2 flow rate through the mixing chamber was constantly kept stable at 1 L/min throughout the measurements, whereas the N_2 flows through the ECs followed the general step profile of 0 mL/min (for 140 sec), 10 mL/min (for 120 sec), 0 mL/min (for 120 sec). The chemical detection of cyclopentane, acetone and toluene across 2 m was done after 57, 62 and 91s of their production (Figure 6a). In this figure, the concentration levels of the three vapors measured at the detector rise at different times due to their different propagation times. The detection times are therefore unsynchronized. From these data, the propagation time of each vapor was measured by subtracting the membrane rise response time (Table 3) from the detection times. The very small signals measured before 100 s correspond to the chemical residues due to manual injection of the liquid analytes within the ECs and correspond to system noise.

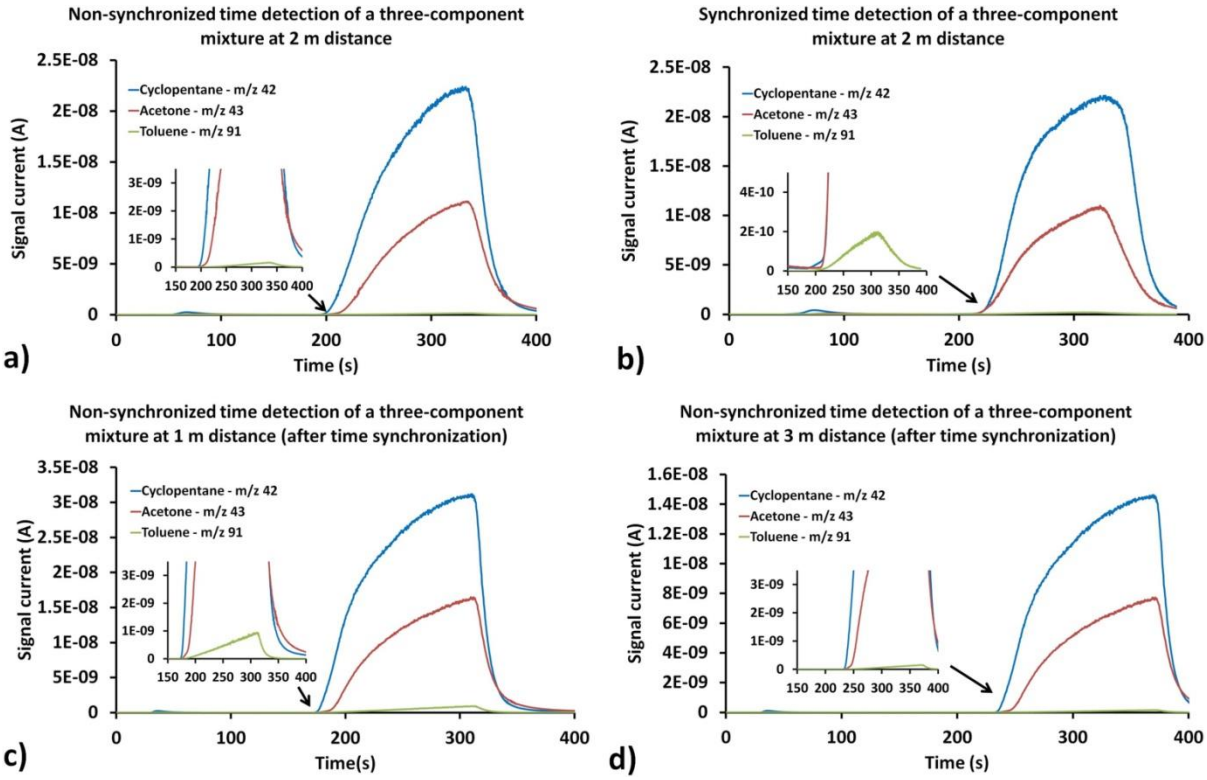

Figure 6. a) Experimental data obtained from the transmission of a three-component gas mixture (cyclopentane, acetone, toluene) within a tubular environment with ID of 20 mm and over a distance of 2 m, b) Repetition of the same transmission experiment with modified release times so that signals detection was done simultaneously at the reference detector. c) Repetition of the transmission experiment for 1 m. Detection time de-synchronization of the 2 m synchronized pulses, d) Odor transmission experiment at a distance of 3 m. Detection time desynchronization of the 2 m synchronized pulses.

In order to synchronize the mass spectrometric detection of these compounds (Figure 6b), the MFCs which control the flow rates through the ECs were programmed to release chemical vapor flows of the selected analytes in the carrier gas stream of the MC at different temporal points. Toluene (lowest vapor pressure and slowest propagator) was transmitted first, followed by acetone (after 29 s) and finally cyclopentane (highest vapor pressure and fastest propagator) was transmitted 5 s after the acetone release. This new transmission

protocol was then used to investigate signal detection time synchronization for the distances 1 m (Figure 6c) and 3 m (Figure 6d). The data obtained showed that for exactly the same operational conditions (flow rates through the MC and ECs, sample load – quantity and concentration, temperature, physical positioning of the odor emitter in relation to the MS, etc.), the detected chemicals previously detected in a synchronized way, have now lost their coherence. There is thus a unique point in space for which measured detection times for a given transmission protocol of these three vapors are coincident. The data show that specific molecular information could be encrypted in certain positions in a confined space and act as a security key of certain level of information during olfactory communication schemes (e.g. a multilevel chemical alphabet for security and military applications or the transmission of odor signals in an entertainment hall, a virtual reality cage or for advisement purposes from an odor transmitter to the human nose - receiver).

4. CONCLUSIONS

In order to study scent molecular communications which will allow us to perform odor transmission experiments over gas channels or odor networks, an odor emitter was designed, built, tested and evaluated using a portable MIMS system. The operating principle of the odor emitter is the controlled evaporation of liquid chemical analytes and their diffusion over a carrier gas stream. The generated gas outputs emitted from the OE are gas standards at specific concentrations. Output signals were produced in a controllable and reproducible way (for both single analytes and mixtures) with output concentrations (signal amplitudes) in the range from low ppb to ppm. The analytical factors which affect odor generation were investigated. Odor synthesis and transfer phenomena for different tube geometries (ID and lengths) were studied using MS monitoring.

For a constant flow through the MC, the flow rates through the ECs determine the form of the final output signal of the odor emitter, allowing signal modulation by this means. Flow rate changes through the MC affect the output concentration (having constant flow rates through the ECs) in an exponential way. Increasing flow rates result in the generation of lower concentration outputs with faster detection times. The vapor pressure and boiling point of the liquid analyte and its quantity within the EC affect the performance of the OE. For a given temperature, compounds with increasing vapor pressure values produce higher signal outputs at the reference detector as it can be seen in Figure 6 (signal intensities of cyclopentane, acetone and toluene are analogous to their vapor pressures). Compounds with high boiling point values such as limonene, require heating of the EC in order to provide stable and easily manipulated output signals. Experiments with transmission of olfactory information within two different ID tubes and over 1, 2 and 3 m presented an exponential signal distribution. Olfactory signals showed that could be used to encrypt information and to be a secure future communication medium.

Positive preliminary results were obtained allowing future exploitation of this technology in the entertainment and/or security sector for transmission of coded information (e.g. encoding of digital information onto odor particles). Further mathematical modeling of the communication channel will be necessary to explain odor transmission through different environments. Conventional and new modulation schemes are planned to be tested and evaluated for potential use. Validation experiments of the developed system during odor transmission over conventional Internet networks and odor regeneration on the other side are planned. Experiments with participants to evaluate the human olfactory perception of characteristic transmitted and generated scents alongside parallel video signals will also follow.

ACKNOWLEDGEMENT

The research leading to these results has received funding from the Engineering and Physical Sciences Research Council (EPSRC) under grant agreement: EP/M029425/1 'Creating a Stink - Investigating Olfactory Transport Streams'. The authors gratefully acknowledge Professor Graham Cooks from Purdue University for his assistance and support. Special thanks are due to Mr Jonty Bray and Mr Scott Brereton from MKS Instruments UK Ltd. and to Mr Gareth Blacoe from the Department of Electrical Engineering and Electronics, University of Liverpool for the technical support of this work.

REFERENCES

[1] Nakamoto, T.: Essentials of Machine Olfaction and Taste. Wiley, (2016)

[2] Keller, P.E., Kouzes, R.T., Kangas, L.J., Hashem, S.: Interactive Technology and the New Paradigm for Healthcare. IOS Press, 168-172 (1995)

[3] Gosain, D., Sajwan, M.: Aroma Tells a Thousand Pictures: Digital Scent Technology a New Chapter in IT Industry. Int. J. Curr. Eng. Tech. 4, 2804-2812 (2014)

[4] Sugimoto, S., Segawa, R., Noguchi, D., Bannai, Y., Okada, K.: Presentation Technique of Scents Using Mobile Olfactory Display for Digital Signage. Proc. 13th IFIP TC 13 Int. Conf. Human-Computer Interact. 3, 323–337 (2011)

[5] Matsukura, H., Yoneda, T., Ishida, H.: Smelling Screen: Technique to Present a Virtual Odor Source at an Arbitrary Position on a Screen. Proc. IEEE Virt. Real. 127–128 (2012)

[6] Farsad, N., Guo, W., Eckfold, A.W.: Tabletop Molecular Communication: Text Messages through Chemical Signals. PLOS ONE 8, 1-13 (2013)

[7] Pierobon, M., Akyildiz, I.: Capacity of a diffusion-based molecular communication system with channel memory and molecular noise. IEEE Transactions on Inform. Theor. 59, 942–954 (2013)

[8] Mahfuz, M. U., Makrakis, D., Mouftah, H. T.: On the characterization of binary concentration-encoded molecular communication in nanonetworks. Nano. Commun. Netw. 1, 289–300 (2010)

[9] Nakano, T., Moore, M. J., Wei, F., Vasilakos, A. V., Shuai, J.: Molecular communication and networking: Opportunities and challenges. IEEE Trans. NanoBiosci. 11, 135–148 (2012)

[10] Bush, S. F.: Nanoscale Communication Networks. Artech House: Norwood, MA, (2010)

[11] Cobo L. C., Akyildiz, I.F.: Bacteria-based communication in nanonetworks. Nano Commun. Netw. 1, 244–256 (2010)

[12] Parcerisa Gine L., Akyildiz, I.F.: Molecular communication options for long range nanonetworks. Comput. Netw. 53, 2753–2766 (2009)

[13] Akyildiz, I.F., Brunetti, F., Blazquez, C.: Nanonetworks: A new communication paradigm. Comput. Netw. 52, 2260–2279 (2008)

[14] Darchini K., Alfa, A.S.: Molecular communication via microtubules and physical contact in nanonetworks: A survey. Nano Commun. Netw. 4, 73–85 (2013)

[15] Farsad, N., Eckford, A.W., Hiyama, S., Moritani, Y.: On-chip molecular communication: Analysis and design. IEEE Trans. NanoBiosci. 11, 304–314 (2012)

[16] Srinivas, K.V., Eckford, A.W., Adve, R.S.: Molecular communication in fluid media: The additive inverse Gaussian noise channel. IEEE Trans. Inf. Theory 58, 4678–4692 (2012)

[17] Chen M.-T., Weiss, R.: Artificial cell-cell communication in yeast saccharomyces cerevisiae using signaling elements from arabidopsis thaliana Nat. Biotechnol. 23, 1551–1555 (2005)

[18] Pelosi, P., Zhou, J.J., Ban, L.P., Calvello, M.: Soluble proteins in insect chemical communication. Cell. Mol. Life Sci. 63, 1658–1676 (2006)

[19] Buck, L., Axel, R.: A novel multigene family may encode odorant receptors: a molecular basis for odor recognition. Cell 65, 175-187 (1991)

[20] Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K., Walter, P.: Molecular Biology of the Cell, 5th edition. Garland Science, (2007)

[21] Wyatt, T.D.: Fifty years of pheromones. Nature 457, 262-263 (2009)

[22] Semmelhack, J.L., Wang, J.W.: Select Drosophila glomeruli mediate innate olfactory attraction and aversion. Nature 459, 218–223 (2009)

[23] Hansson, B.S., Stensmyr, M.C.: Evolution of Insect Olfaction. Neuron 72, 698-711 (2011)

[24] Tristram, D. W.: Pheromones and animal behaviour: communication by smell and taste, Cambridge University Press, 2003, 1-36.

[25] Agosta, W.C.: Chemical Communication: The Language of Pheromones. 1st edition W. H. Freeman & Co (1992).

[26] Reddy, G.V.P., Guerrero, A.: Interactions of insect pheromones and plant semiochemicals. Trends Plant Sci. 9, 253 - 261 (2004)

[27] Durand, K., Baudouin, J.-Y., Lewkowicz, D.J., Goubet, N., Schaal, B.: Eye-Catching Odors: Olfaction Elicits Sustained Gazing to Faces and Eyes in 4-Month-Old Infants. PLOS ONE 8, 1-8 (2013)

[28] Justus, K.A., Cardé, R. T.: Flight behavior of males of two moths, Cadra cautella and Pectinophora gossypiella, in homogeneous clouds of pheromone. Physiol. Entomol. 27, 67–75 (2002)

[29] Judd, G.J.R., Gardiner, M.G.T., DeLury, N.C., Karg, G.: Reduced antennal sensitivity, behavioral response, and attraction of male codling moths, Cydia pomonella,

to their pheromone (E,E)-8,10-dodecadien-1-ol following various pre-exposure regimes. Entomol. Exp. Appl. 114, 65-78 (2005)

[30] Hansson, B. S., Van der Pers, J. N. C., Löfqvist, J.: Comparison of male and female olfactory cell response to pheromone compounds and plant volatiles in the turnip moth, *Agrotis segetum*. Physiol. Entomol. 14, 147-55 (1989)

[31] Galizia, C.G., Sachse, S., Mustaparta, H.: Calcium responses to pheromones and plant odors in the antennal lobe of the male and female moth Heliothis virescens. J. Comp. Physiol. A. 186, 1049–63 (2000)

[32] Ueda, H., Kikuta, Y., Matsuda, K.: Plant communication Mediated by individual or blended VOCs. Plant Signal Behav. 1, 222-226 (2012)

[33] Stacey, N.E., Wisenden, B.D., Sorensen, P.W.: Chemical communication in fish Chemical Ecology, Encyclopedia of Life Support Systems, Eolss Publishers Co. Ltd., Oxford, UK, (2009)

[34] Brown, Jr.W.L., Eisner, T. Whittaker, R.H.: Allomones and kairomones: transspecific chemical messengers. BioScience 20, 21-22 (1970)

[35] Kim, J., Kim, D., Han, D., Byun, H., Ham, Y., Jung, W., Park, J., Oh, S.: A Proposal Representation, Digital Coding and Clustering of Odor Information. IEEE 872-877 (2006)

[36] Ma, M.: Encoding olfactory signals via multiple chemosensory systems. Critical Reviews in Biochem. and Mol. Biol. 42, 463-480 (2007)

[37] Mukai, M., Maruo, K., Kikuchi, J.-I., Sasaki, Y., Hiyama, S., Moritani, Y., Suda, T.: Propagation and amplification of molecular information using a photoresponsive molecular switch. Supramol. Chem. 21, 284–291 (2009)

[38] Matsukura, H., Yoneda T., Ishida, H.: Smelling screen: development and evaluation of an olfactory display system for presenting a virtual odor source. IEEE Trans. Visualiz. and Comput. Graph. 19, 606-615 (2013)

[39] Morie, J.F., Luigi, D., Lathan, C., Pettersen, M., Vice, J.M.: Scent Delivery Device and Method of Simulating Scent in a Virtual Environment. U.S. Patent 7484716 B2, (2009)

[40] Russell, R.A.: Odour detection by mobile robots. Singapore, World Scientific (1999)

[41] Cole, M., Racz, Z., Gardner, J.W., Pearce, T.C.: A novel biomimetic infochemical communication technology: From insects to robots. Proc. IEEE Sensors 1–4 (2012)

[42] Mukai, M., Maruo, K., Kikuchi, J.-I., Sasaki, Y., Hiyama, S., Moritani, Y., Suda, T.: Propagation and amplification of molecular information using a photoresponsive molecular switch. Supramol. Chem. 21, 284–291 (2009)

[43] Giannoukos, S., Brkić, B., Taylor, S., Marshall A., Verbeck, G.F.: Chemical sniffing instrumentation for security applications. Chem. Reviews 116, 8146-8172 (2016)

[44] Díaz-Maroto, M.C., Guchu, E., Castro-Vázquez, L., de Torres, C., Pérez-Coello, M.S.: Aroma-active compounds of American, French, Hungarian and Russian oak woods, studied by GC-MS and GC-O. Flavour Fragr. J. 23, 93–98 (2008)

[45] Lo, Y.C.M., Koziel, J.A., Cai, L., Hoff, S.J., Jenks, W.S., Xin, H.: Simultaneous chemical and sensory characterization of volatile organic compounds and semi-volatile organic compounds emitted from swine manure using solid phase microextraction and multidimensional Gas Chromatography-Mass Spectrometry-Olfactometry. J. Environ. Qual. 37, 521–534 (2008)

[46] Cai, L., Koziel, J.A., Lo, Y.C., Hoff, S.J.: Characterization of volatile organic compounds and odorants associated with swine barn particulate matter using solid-phase

microextraction and gas chromatography-mass spectrometry-olfactometry. J. Chromatogr. A 1102, 60–72 (2006)

[47] Marković, K., Vahčić, N., Ganić, K.K., Banović, M.: Aroma volatiles of tomatoes and tomato products evaluated by solid-phase microextraction. Flavour Fragr. J. 22, 395–400 (2007)

[48] Petra, S., Peter, S.: Characterization of the key aroma compounds in soy sauce using approaches of molecular sensory science. J. Agric. Food Chem. 55, 6262–6269 (2007)

[49] Martí, M.P., Mestres, M., Sala, C., Busto, O., Gausch, C.: Solip-phase microextraction and gas chromatography olfactometry analysis of successively diluted samples. A new approach of the aroma extract dilution analysis applied to the characterization of wine aroma. J. Agric. Food Chem. 51, 7861–7865 (2003)

[50] Marsili, R.: Flavor, fragrance and odor analysis, CRC Press, Inc. New York (2002)

[51] Brattoli, M., Cisternino, E., Dambruoso, P.R., de Gennaro, G., Giungato, P., Mazzone, A., Palmisani, J., Tutino, M.: Gas Chromatography Analysis with Olfactometric Detection (GC-O) as a Useful Methodology for Chemical Characterization of Odorous Compounds. Sensors 13, 16759-16800 (2013)

[52] Naudé, Y., Rohwer, E.R.: Investigating the coffee flavour in South African Pinotage wine using novel offline olfactometry and comprehensive gas chromatography with time of flight mass spectrometry. J. Chromatogr. A 1271, 176–180 (2013)

[53] Etiévant, P.X., Callement, G., Langlois, D., Issanchou, S., Coquibus, J.N.: Odor intensity evaluation in gas chromatography-olfactometry by finger span method. Agric. Food Chem. 47, 1673–1680 (1999)

[54] Fur, Y., Mercurio, V., Moio, L., Blanquet, J., Meunier, J.M.: A new approach to examine the relationships between sensory and gas chromatography-olfactometry data

using generalized procrustes analysis applied to six French Chardonnay wines. J. Agric. Food Chem. 51, 443–452 (2003)

[55] Benzo, M., Gilardoni, G., Gandini, C., Caccialanza, G., Finzi, P.V., Vidari, G., Abdo, S., Layedra, P.: Determination of the threshold odor concentration of main odorants in essential oils using gas chromatography–olfactometry incremental dilution technique. J. Chromatogr. A 1150, 131–135 (2007)

[56] Eyres, G., Marriott, P. J., Dufour, J. P.: The combination of gas chromatography-olfactometry and multidimensional gas chromatography for the characterization of essential oils. J. Chromatogr. A. 1150, 70–77 (2007)

[57] Márquez, V., Martínez, M., Guerra, M., Fariña, L., Boido, E., Dellacassa, E.: Characterization of aroma-impact compounds in yerba mate (Ilex paraguariensis) using GC-olfactometry and GC-MS. Food Res. Int. 53, 808–815 (2013)

[58] Williams, J., Stönner, C., Wicker, J., Krauter, N., Derstroff, B., Bourtsoukidis, E., Klüpfel, T., Kramer, S.: Cinema audiences reproducibly vary the chemical composition of air during films, by broadcasting scene specific emissions on breath Nature Scientific Reports 6:25464, 1-10 (2016)

[59] Craven, M. A., Gardner, J. W., Bartlett, P. N.: Electronic noses-development and future prospects. Trends Anal. Chem. 15, 486–493 (1996)

[60] Sobel, N., Prabhakaran, V., Desmond, J. E., Glover, G. H., Goode, R. L., Sullivan, E. V., Gabrieli, J. D.: Sniffing and smelling: separate subsystems in the human olfactory cortex. Nature 392, 282-286 (1998)

[61] Zhao, K., Dalton, P., Yang, G.C., Scherer, P.W.: Numerical modelling of turbulent and laminar air flow and odorant transport during sniffing in the human and rat nose Chem. Senses 31, 107-118 (2006)

[62] Weinhold, I., Mlynski, G.: Numerical simulation of air flow in the human nose Eur. Arch. Otorhinolaryngol. 261, 452-455 (2004)

[63] Zhao, K., Scherer, P.W., Hajiloo, S.A., Dalton, P.: Effect of anatomy on human nasal air flow and odorant transport patterns. Chem. Senses 29, 365-379 (2004)

[64] Bushdid, C., Magnasco, M.O., Vosshall, L.B., Keller, A.: Humans can discriminate more than 1 trillion olfactory stimuli. Science 343, 1370-1372 (2014)

[65] Ishikawa, S., Nakayama, T., Watanabe, M., Matsuzawa, T.: Flow mechanisms in the human olfactory groove, Numerical simulation of nasal physiological respiration during inspiration, expiration and sniffing. Arch. Otolaryngol. Head Neck Surg. 135, 156-162 (2009)

[66] McClennen, W.H., Vaughn, C.L., Cole, P.A., Sheya, S.N., Wager, D.J., Mott, T.J., Dworzanski, J.P., Arnold, N.S., Meuzelaar H.L.C.: Roving GC/MS: Mapping VOC gradients and trends in space and time. Field Anal. Chem. Technol. 1, 109−116 (1996)

[67] Naganowska-Nowak, A., Konieczka, P., Przyjazny A., Namiesnik, J.: Development of techniques of generation of gaseous standard mixtures. Crit. Rev. Anal. Chem. 35, 31-55 (2005)

[68] Greenhouse, S., Andrawes, F.: Generation of gaseous standards using exponential dilution flasks in series. Anal. Chim. Acta 236, 221-226 (1990)

[69] Fowlis, I. A., Scott, P. W.: A vapour dilution system for detector calibration. J. of Chromatogr. 2, 1-10 (1963)

[70] Namiesnik, J.: Generation of standard gaseous mixtures. J. of Chromatogr. 300, 79-108 (1984)

[71] Koziel, J.A., Martos, P.A., Pawliszyn, J.: System for the generation of standard gas mixtures of volatile and semi-volatile organic compounds for calibrations of solid-phase microextraction and other sampling devices J. of Chromatogr. A 1025, 3-9 (2004)

[72] Slominska, M., Konieczka, P., Namiesnik, J.: Standard gas mixtures-indispensable reference materials in the analysis of gaseous media. Trends in Anal. Chem. 29, 419-429 (2010)

[73] Konieczka, P., Namieśnik, J., Biernat, J.F.: Generation of standard gaseous mixtures by thermal decomposition of surface compounds: Standard mixtures of thiols. J. Chromatogr. A 540, 449-455 (1991)

[74] Jardine, K.J., Henderson, W.H., Huxman, T.E., Abrell, L.: Dynamic solution injection: a new method for preparing pptv-ppbv standard atmospheres of volatile organic compounds. Atmos. Meas. Tech. 3, 1569–1576 (2010)

[75] Brito, J., Zahn, A.: An unheated permeation device for calibrating atmospheric VOC measurements. Atmos. Meas. Tech. 4, 2143–2152 (2011)

[76] National Physical Laboratory, Gas standards and measurements, http://www.npl.co.uk/.

[77] Przyk, E., Świtaj-Zawadka, A., Konieczka, P., Szczygelska-Tao, J., Biernat, J. F., Namieśnik, J.: Thermal decomposition of surface compounds for the generation of small quantities of acetaldehyde: Calibration of a thermal desorption–gas chromatography–flame ionization detection. Anal. Chim. Acta 488, 89-96 (2003)

[78] Hafkenscheid, T., Baldan, A., Quincey, P., Cortez, L., Dias, F., Brown, R., Wright, M., Gerboles, M., Saunders, K.: A technical review of the feasibility of producing certified reference materials for the measurement of gaseous pollutants in ambient air. Atm. Environ. 39, 3947-3965 (2005)

[79] Xiong, G., Pawliszyn, J.: Microwave-assisted generation of standard gas mixtures. Anal. Chem.74, 2446–2449 (2002)

[80] Przyk, E., Konieczka, P., Szczygelska-Tao, J., Teschner, R., Biernat, J.F., Namiesnik, J.: Use of porous glass and silica gel as support media of a surface compound for

generation of analytes in gaseous standard mixtures. A new method for the determination of the amount of analyte generated. J. Chromatogr. A 928, 99–108 (2001)

[81] Ballesta, P.P., Baldan, A., Cancelinha, J.: Atmosphere generation system for the preparation of ambient air volatile organic compound standard mixtures. Anal. Chem. 71, 2241–2245 (1999)

[82] Li, Y., Taffner, T., Bischoff, M., Niemeyer, B.: Test gas generation from pure liquids: an application –oriented overview of methods in a nutshell. Inter. J. of Chem. Eng. Article ID 417029, 1-6 (2012)

[83] Gautrois, M., Koppmann, R.: Diffusion technique for the production of gas standards for atmospheric measurements, J. Chromatogr. A, 848, 239–249 (1999)

[84] Cussler, E.L.: Diffusion: mass transfer in fluid systems. Cambridge University Press, (2009)

[85] Llatser, I., Cabellos-Aparicio, A., Pierobon, M., Alarcon, E.: Detection techniques for diffusion-based molecular communication. IEEE J. Sel. Areas Commun. 31, 726–734 (2013)

[86] Statheropoulos, M., Pallis, G.C., Mikedi, K., Giannoukos, S., Agapiou, A., Pappa, A., Cole, A., Vautz, W., Thomas, C.L.P.: Dynamic vapor generator that simulates transient odor emissions of victims entrapped in the voids of collapsed buildings. Anal. Chem. 86, 3887–3894 (2014)

[87] Q-Technologies Ltd., Liverpool, UK, http://q-technologies.co.uk/.

[88] Giannoukos, S., Brkić, B., Taylor, S., France, N.: Monitoring of human chemical signatures using membrane inlet mass spectrometry. Anal. Chem. 86, 1106−1114 (2014)

[89] Giannoukos, S., Brkić, B., Taylor S., France, N.: Membrane inlet mass spectrometry for homeland security and forensic applications. J. Am. Soc. Mass Spectrom. 26, 231-239 (2015)

[90] Giannoukos, S., Brkić, B., Taylor S.: Analysis of chlorinated hydrocarbons in gas phase using a portable membrane inlet mass spectrometer. Anal. Methods 8, 6607-6615 (2016)

[91] Giannoukos, S., Antony Joseph, M.J., Taylor, S.: Portable mass spectrometry for the direct analysis and quantification of volatile halogenated hydrocarbons in the gas phase. Anal. Methods 9, 910-920 (2017)

[92] Owlstone Ltd., http://www.owlstonenanotech.com/.

Graphical Abstract